BS

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/085,982	10/24/2001	Nir Hacohen	WIBL-P01-548	7046

28120 7590 11/01/2004

ROPES & GRAY LLP
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER	
SMITH, CAROLYN L	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 11/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/085,982	HACOHEN ET AL.	
	Examiner	Art Unit	
	Carolyn L Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,9,51 and 59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,9,51 and 59* is/are rejected.

7)☒ Claim(s) *5 and 59* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *09132004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission, filed 8/11/04, has been entered.

Amended claims 1, 5, 9, and 51; new claim 59; and cancelled claims 2-4, 6-8, 10-50, and 52-58, filed 8/11/04, are acknowledged.

It is noted that the 892 form, mailed 10/29/03, inadvertently listed the Source as "Genomics" when the actual publication name is "Emerging Infectious Diseases". The correct citation is being furnished in the current 892 form.

Claims herein under examination are 1, 5, 9, 51, and 59.

Claim Objections

Claims 5 and 59 are objected to because of the following minor informality: "an immunogenic components" does not make grammatical sense as the word "an" represents a singular form while the word "components" represents a plural form. Appropriate correction is requested.

Claims Rejected Under 35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5, 9, 51, and 59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claims 1, 5, 9, 51, and 59 recite the phrases "wherein increased or decreased expression [...] aids in identification of the infecting pathogen" (claims 1, 5, 51) and "wherein increased or decreased expression aids in diagnosis of infection" (claims 9 and 59) which are vague and indefinite. It unclear what degree of increased or decreased expression is required for such aiding as one skilled in the art would realize that some variation is likely due to experimental variation or background noise. Clarification of the metes and bounds of the claim via clearer claim wording is requested.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. (e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 5, 9, 51, and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cummings et al. (Genomics, Vol. 6, No. 5, Sept-Oct 2000, pages 513-525) in view of Exley et al. (US 2002/0164331 A1).

Cummings et al. describe methods of using host gene microarrays to explore gene level expressions that follow infection of a microbial pathogen (abstract). Cummings et al. describe host profiling as a way to identify gene expression signatures unique for each pathogen to be used as a tool for diagnosis, prognosis, and clinical management of infectious disease (abstract). The instant specification states a "stimulus" includes bacteria, fungi, viruses, or components thereof (page 5, first paragraph). On page 15, lines 20-22, the instant specification refers to "stimulus-specific" and "pathogen-specific" genes as genes that are "specifically-regulated by a pathogen, pathogen-class or component thereof". Therefore, the unique gene expression signature due to pathogen infection mentioned by Cummings et al. is reasonably interpreted to include "pathogen-specific" genes as stated in claim 1. Cummings et al. describe that gene expression profiling of host-pathogen interactions are emerging in the science field (page 514, col. 1, first paragraph). Cummings et al. describe measuring relative gene expression and

analyzing experiments with red (positive values or increased expression) and green (negative values or decreased expression) and black (near zero values or no expression) (Figure 1 caption). Cummings et al. describe examining infected cultured cells (page 520, col. 1, fifth paragraph) which is reasonably interpreted as cells that have come into contact with a pathogen. Cummings et al. describe preparing and purifying mRNA from eukaryotic cells (including humans, a type of mammal) to be used in hybridization experiments with microarrays (Figure 1; page 514, col. 2, second paragraph; and page 515, col. 1, first paragraph and col. 2, second paragraph). Cummings et al. describe isolating and labeling RNA from microbial samples as well (page 518, col.2, third paragraph). Cummings et al. describe labeling mRNA in the microarray methodology (page 515, col. 1, first paragraph). Cummings et al. describe performing a cross-species comparison of many different pathogens (page 517, col. 1, second paragraph) which represent reference gene expression profiles (as the instant claims do not mention that the reference gene profile is from the same organism), as stated in instant claims 1, 5, 9, 51, and 59. Cummings et al. describe monitoring gene expression in *M. tuberculosis*, a pathogen, while it infects cultured monocytes (page 518, col. 1, second paragraph). Cummings et al. describe genes that are specifically expressed during infection (page 518, col.2, third paragraph). Cummings et al. describe comparing arrays to monitor gene expression in primary human fibroblasts infected (infected human) with human CMV in reference to uninfected cells (control) and noting fourfold differences between infected and uninfected human genes (page 520, col. 2, first paragraph) which represents an increased or decreased expression of at least one pathogen-specific gene relative to expression of the pathogen-specific gene in a reference (uninfected control) gene expression profile, as stated in all instant claims. Cummings et al. describe

examining HIV-1 infection in CD4-positive T cells and noting differential expression in 20 human genes (page 520, col. 2, second paragraph). Cummings et al. describe examining response to host cells to infection with bacterial pathogens (page 520, col. 2, third paragraph). Cummings et al. describe comparison of gene expression profiling data from human monocytes infected by different strains of virus (page 521, col. 1, third paragraph) which is interpreted to be an analysis of gene profiles relative to other reference profiles to identify specific genes for a particular pathogen. Cummings et al. describe microarrays used in measuring responses of cultured cells to distinct external stimuli (page 521, col. 2, second paragraph). Cummings et al. describe measuring gene expression in leukocytes to find signatures diagnostic of infection by specific pathogens (page 521, col. 2, third paragraph). Cummings et al. describe using these host gene expression signatures as diagnostic markers (or probes) of infection (page 521, col. 2, fourth paragraph). Cummings et al. describe identification of gene expression profiles common to many different pathogens (page 522, col. 1, second paragraph). Cummings et al. do not specifically describe dendritic or immature dendritic cells (claims 1, 5, 9, 51, and 59).

Exley et al. describe T cells that are lymphocytes that participate in multiple cell-mediated immune reactions, such as recognition and destruction of infected or cancerous cells (paragraph 0004). Exley et al. describe diagnostic methods involving T cells (abstract). It is noted that Applicants supplied an online Medical dictionary definition of dendritic cell that includes a T lymphocyte. Exley et al. describe using immature and mature dendritic cells in various experiments, including DNA microarrays (paragraphs 0117, 0220, 0224, 0245, 0249, 0251). Exley et al. describe contacting T cells with an antigen or antigen presenting cells wherein the antigen is an infectious pathogen (paragraphs 0043 and 0126). Exley et al. describe

identifying gene expression patterns using DNA microarrays and determining expression profiles with a control (reference) (paragraphs 0217, 0219, and 0220). Exley et al. describe isolating and labeling RNA from the T cells that were then hybridized on DNA microarray chips (paragraph 0229). Exley et al. describe genes that are differentially expressed (paragraph 0113 and Figure 25A) followed by determining and comparing changes in gene expression of specific genes identified in Figure 25A (paragraph 0114 and Figures 26A and B).

Cummings et al. state the interaction between a microbial pathogen and a host is the underlying basis of infectious disease (page 513, col. 1, first paragraph). Cummings et al. also state that understanding the details of this interaction will help us identify virulence-associated microbial genes and host defense strategies and their regulated (page 513, col. 1, first paragraph). Cummings et al. state this information will guide the design of a new generation of medical tools (page 513, col. 1, first paragraph). Cummings et al. state explaining life at a molecular level is slow because gene function understanding lags behind and that high throughput methods are required (page 513, col. 1, second paragraph to col. 2, first paragraph). Cummings et al. state microarray-based approaches hold exceptional promise and will make substantial contributions for studying infectious disease (page 513, col. 2, third paragraph). Cummings et al. state the goals of functional genomics and microarray technology in infectious diseases will require additional technology, extensive data collection, and sophisticated computational tools (col. 522, col. 1, fourth paragraph). Exley et al. state there is a need to specifically monitor T cells in mammals for infections (paragraph 0014). As Cummings et al. state the goals of identifying and diagnosing host-pathogen interactions (page 522, col. 1, fourth paragraph), one of ordinary skill in the art would have been motivated to perform such microarray technology on cells, genes, and

pathogens already known to be specific for a particular pathogen (abstract). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use the dendritic cells, such as those noted by Exley et al., in the microarray technology suggested by Cummings et al. in order to help further identify genes unique for each pathogen. One would have a reasonable expectation of success since T cells are already known to play a role in recognizing infected cells (Exley et al., paragraph 0004).

Thus, Cummings et al., in view of Exley et al. motivate the instant invention.

Applicants state a passage in Cummings et al. that "host profiling might [...] identify gene expression signatures unique pathogen" (abstract) and concludes the goal for these experiments has not been realized. This statement is acknowledged; however, as unique gene expression signatures have been created for other scientific experiments and since microarray technology had previously been performed on dendritic cells, the expectation for success appears to be quite high for such an endeavor, as described in the rejection above. Applicants differentiate between definitions of the phrase "dendritic cells" (immune cells versus cells with dendrites). Although the phrase could be broadly interpreted to be either definition, it is acknowledged that the statement on page 1, lines 14-16, of the specification appears to refer to the immune cell definition of the phrase "dendritic cell". A different prior art was added to the 35 US 103 rejection in order to further address the limitations and amendments of the instant claims.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

October 18, 2004

Ardin H. Marschel 10/27/04
ARDIN H. MARSCHEL
PRIMARY EXAMINER